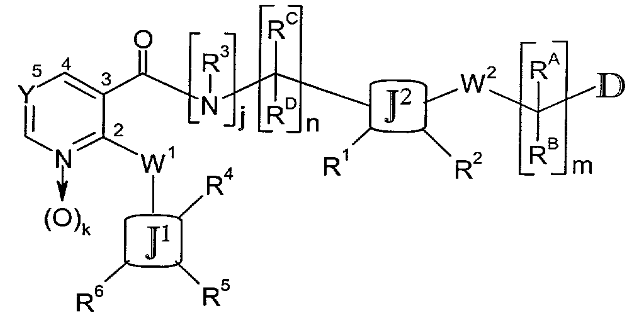
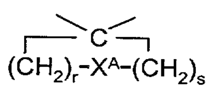
ABSTRACT OF THE DISCLOSURE

Compounds useful as inhibitors of PDE4 in the treatment of diseases regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructuive pulmonary disease, of the formula:

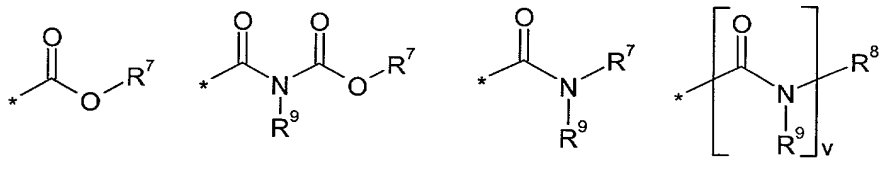


wherein j is 0 or 1, provided that when **j** is 0, **n** must be 2; **k** is 0 or 1; **m** is 1, 2, or 3; **n** is 1 or 2; $\mathbf{W^1}$ and $\mathbf{W^2}$ are –O–; –S(=O)$_t$– , where t is 0, 1, or 2, or –N(R^3)–; **Y** is =C(R^1_a)—, or -[N⇒(O)$_k$]– where **k** is 0 or 1; $\mathbf{R^1_a}$ is —H, —F, —Cl, —CN, —NO_2, —(C_1-C_4) alkyl, –(C_2-C_4) alkynyl, fluorinated-(C_1 -C_3) alkyl, fluorinated-(C_1 -C_3) alkoxy, -OR^{16}, or –C(=O)$NR^{22}_aR^{22}_b$; $\mathbf{R^A}$ **and** $\mathbf{R^B}$ are –H, –F, –CF_3, –(C_1-C_4) alkyl, –(C_3-C_7) cycloalkyl, phenyl, or benzyl substituted by 0-3 R^{10}; or $\mathbf{R^A}$ **and** $\mathbf{R^B}$ are taken together to form a spiro moiety

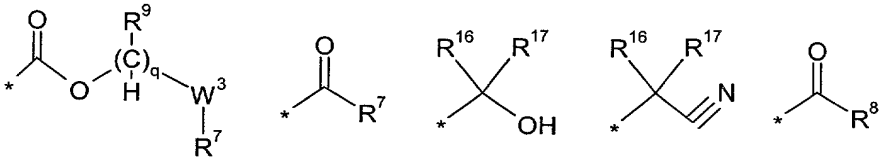


where **r and s** are 0-4 provided r + s is ≥1 but not > 5; and $\mathbf{X^A}$ is –CH_2–, –CHF, –CF_2, –NR^{15}–, –O–, or -S(=O)$_t$–, where **t** is 0, 1; $\mathbf{R^C}$ **and** $\mathbf{R^D}$ are the same as R^A and R^B except that one of them must be –H; $\mathbf{R^1}$ **and** $\mathbf{R^2}$ are –H, –F, –Cl, –CN, –NO_2, -(C_1-C_4) alkyl, –(C_2-C_4) alkynyl, fluorinated–(C_1 -C_3) alkyl, –OR^{16}, or -C(=O)$NR^{22}_aR^{22}_b$; $\mathbf{R^3}$ is -H, –(C_1-C_3) alkyl, phenyl, benzyl, or –OR^{16}; $\mathbf{R^4}$, $\mathbf{R^5}$ **and** $\mathbf{R^6}$ are (a) –H, –F, –Cl, -(C_2-C_4) alkynyl, -R^{16}, –OR^{16}, –S(=O)$_pR^{16}$, -C(=O)R^{16}, -C(=O)OR^{16}, –OC(=O)R^{16}, –CN, -NO_2, -C(=O)$NR^{16}R^{17}$, –OC(=O)$NR^{16}R^{17}$, -NR^{22}_aC(=O)$NR^{16}R^{17}$, -NR^{22}_aC(=NR^{12})$NR^{16}R^{17}$, -NR^{22}_aC(=NCN)$NR^{16}R^{17}$, -NR^{22}_aC(=N-NO_2)$NR^{16}R^{17}$, -C(=NR^{22}_a)$NR^{16}R^{17}$, -CH_2C(=NR^{22}_a)$NR^{16}R^{17}$, –OC(=NR^{22}_a)$NR^{16}R^{17}$, –OC(=N–NO_2)$NR^{16}R^{17}$, -$NR^{16}R^{17}$, -$CH_2NR^{16}R^{17}$, -NR^{22}_aC(=O)R^{16}, -NR^{22}_aC(=O)OR^{16}, =NOR^{16}, –NR^{22}_aS(=O)$_pR^{17}$ -S(=O)$_pNR^{16}R^{17}$; or –CH_2C(=NR^{22}_a)$NR^{16}R^{17}$; where **p** is 0, 1, or 2; (b) -(C_1-C_4) alkyl or -(C_1-C_4) alkoxy substituted by 0-3 of –F or –Cl; or 0 or 1 of (C_1-C_2) alkoxycarbonyl–, (C_1-C_2) alkylcarbonyl–, or (C_1-C_2) alkylcarbonyloxy–; or (c) phenyl, benzyl, furanyl, tetrahydrofuranyl, oxetanyl, thienyl, tetrahydrothienyl, pyrrolyl, pyrrolidinyl, oxazolyl, oxazolidinyl, isoxazolyl, isoxazolidinyl, thiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl,

pyrazolyl, pyrazolidinyl, oxadiazolyl, thiadiazolyl, imidazolyl, imidazolidinyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, piperidinyl, piperazinyl, triazolyl, triazinyl, tetrazolyl, pyranyl, azetidinyl, morpholinyl, parathiazinyl, indolyl, indolinyl, benzo[*b*]furanyl, 2,3-dihydrobenzofuranyl, 2-*H*-chromenyl, chromanyl, benzothienyl, 1-*H*-indazolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, or purinyl, all substituted by 0-2 of R^{14}, or (d) **R^5 and R^6** are taken together to form a moiety of partial Formulas (1.3.1) through (1.3.15); **D** is a group of partial Formulas (1.1.1) through (1.1.9):



(1.1.1) (1.1.2) (1.1.3) (1.1.4)



(1.1.5) (1.1.6) (1.1.7) (1.1.8) (1.1.9)

where **q** is 1-3, provided where q is 2 or 3, R^9 is –H; **v** is 0-1; **W^3** is –O–, –N(R^9)–, or -OC(=O)–; **R^7** is (a) –H; (b) –(C_1-C_6) alkyl, –(C_2-C_6) alkenyl, or –(C_2-C_6) alkynyl, all substituted by 0-3 of R^{10}; (c) –$(CH_2)_u$-(C_3-C_7) cycloalkyl where **u** is 0-2, substituted by 0-3 of R^{10}; or (d) phenyl or benzyl substituted by 0-3 of R^{10}; **R^8** is (a) tetrazol-5-yl, 1,2,4-triazol-3-yl, 1,2,4-triazol-3-on-5-yl, 1,2,3-triazol-5-yl, imidazol-2-yl, imidazol-4-yl, imidazolidin-2-on-4-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-on-3-yl, 1,2,4-oxadiazol-5-yl, 1,2,4-oxadiazol-3-on-5-yl, 1,3,4-oxadiazolyl, 1,3,4-oxadiazol-2-on-5-yl, oxazolyl, isoxazolyl, pyrrolyl, pyrazolyl, succinimidyl, glutarimidyl, pyrrolidonyl, 2-piperidonyl, 2-pyridonyl, 4-pyridonyl, pyridazin-3-onyl, thiadiazolyl, parathiazinyl; (b) indolyl, indolinyl, isoindolinyl, benzo[*b*]furanyl, 2,3-dihydrobenzofuranyl, 2-*H*-chromenyl, chromanyl, benzothienyl, 1*H*-indazolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzotriazolyl, benzotriazinyl, quinazolinyl, quinoxalinyl, pyrazolo[3,4-*d*]pyrimidinyl, pyrimido[4,5-*d*]pyrimidinyl, imidazo[1,2-*a*]pyridinyl, pyridopyridinyl, pteridinyl, or purinyl, all optionally substituted on a carbon atom by R^{14}, on a nitrogen atom by R^{15} and all tautomer forms thereof, or on a sulfur atom by 0-2 oxygen atoms; **R^9** is –H, –(C_1-C_4) alkyl, -(C_3-C_7) cycloalkyl, phenyl, benzyl, -C(=O)OR^{16}, –C(=O)R^{16}, –OR^{16}, -(C_1-C_2) alkyl–OR^{16}, or –(C_1-C_2) alkyl–C(=O)OR^{16}; or (c) -O-P(=O)$(OH)_2$ (phosphoric), -PH(=O)OH (phosphinic), -P(=O)$(OH)_2$ (phosphonic), -[P(=O)(OH)–O(C_1-C_4) alkyl] (alkylphosphono), -P(=O)(OH)-O(C_1-C_4) alkyl) (alkylphosphinyl), –P(=O)$(OH)NH_2$

(phosphoramido), -P(=O)(OH)NH(C_1-C_4) alkyl and -P(=O)(OH)NHR^{25} (substituted phosphoramido), -O-S(=O)$_2$OH (sulfuric), –S(=O)$_2$OH (sulfonic), –S(=O)$_2$NHR^{26} or -NHS(=O)$_2$R^{26} (sulfonamido) where R^{26} is –CH_3, –CF_3, or *o*-toluyl, and acylsulfonamido selected from the group consisting of -C(=O)NHS(=O)$_2$R^{25}, –C(=O)NHS(=O)$_2$NH$_2$, -C(=O)NHS(=O)$_2$(C_1-C_4) alkyl, -C(=O)NHS(=O)$_2$NH(C_1-C_4) alkyl, -C(=O)NHS(=O)$_2$N[(C_1-C_4) alkyl]$_2$, -S(=O)$_2$NHC(=O)(C_1-C_4) alkyl, –S(=O)$_2$NHC(=O)NH$_2$, -S(=O)$_2$NHC(=O)NH(C_1-C_4) alkyl, -S(=O)$_2$NHC(=O)N[(C_1-C_4) alkyl]$_2$, –S(=O)$_2$NHC(=O)R^{25}, -S(=O)$_2$NHCN, -S(=O)$_2$NHC(=S)NH$_2$, –S(=O)$_2$NHC(=S)NH(C_1-C_4) alkyl, -S(=O)$_2$NHC(=S)N[(C_1-C_4) alkyl]$_2$, or -S(=O)$_2$NHS(=O)$_2$R^{25}, where **R^{25}** is –H, –(C_1-C_4) alkyl, phenyl, or –OR^{16}; $\mathbb{J}^1$ and $\mathbb{J}^2$ are a moiety comprising a saturated or unsaturated carbon ring system that is 3- to 7-membered monocyclic, or that is 7- to 12-membered, fused or discontinuous, polycyclic; wherein optionally one carbon atom of said carbon ring system may be replaced by a heteroatom selected from N, O, and S; and where N is selected, optionally a second carbon atom thereof may be replaced by a heteroatom selected from N, O, and S; or a pharmaceutically acceptable salt thereof.